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DOCUMENT-IDENTIFIER: US 6183753 B1
TITLE: Recombinant chimeric virus and uses thereof

Brief Summary Text (13):
A relevant avian pathogen that is a target for HVT vectoring is Infectious Laryngotracheitis virus (ILTV). ILTV is a member of the herpesviridiae family, and this pathogen causes an acute disease of chickens which is characterized by respiratory depression, gasping and expectoration of bloody exudate. Viral replication is limited to cells of the respiratory tract, where in the trachea the infection gives rise to tissue erosion and hemorrhage. In chickens, no drug has been effective in reducing the degree of lesion formation or in decreasing clinical signs. Vaccination of birds with various modified forms of the ILT virus derived by cell passage and/or tedious regimes of administration have conferred acceptable protection in susceptible chickens. Because of the degree of attenuation of current ILT vaccines care must be taken to assure that the correct level of virus is maintained; enough to provide protection, but not enough to cause disease in the flock.

Detailed Description Text (25):
The invention further provides a recombinant herpesvirus of turkeys whose viral genome contains foreign DNA encoding an antigenic polypeptide which is from Marek's disease virus (MDV), Newcastle disease virus (NDV), infectious laryngotracheitis virus (ILTV), infectious bronchitis virus (IBV) or infectious bursal disease virus (IBDV).

Detailed Description Text (35):
The invention further provides a recombinant herpesvirus of turkeys which contains a foreign DNA sequence encoding an antigenic polypeptide from infectious laryngotracheitis virus. It is preferred that the antigenic polypeptide is ILTV glycoprotein gB, ILTV gD or ILTV gI.

Detailed Description Text (214):
Plasmid 852-52.II4 was constructed for the purpose of generating recombinant chimeric HVT/MDV vaccine expressing a foreign DNA sequence. The infectious laryngotracheitis (ILT) virus glycoprotein D (gD) and glycoprotein I (gI) genes are expressed under the control of the ILT virus gD and gI promoters. The HVT DNA is an AscI subclone of cosmid 407-32.1C1 (see FIGS. 2 and 5). The cosmid was constructed by joining restriction fragments (Sambrooks, et al., 1989) from the following sources. The vector is an approximately 2000 base pair AscI fragment constructed from a 2000 base pair AatII to PvuII fragment of pNEB193 (New England Biolabs, Inc.) blunt ended with Klenow DNA polymerase and AscI linkers inserted. The HVT fragment is an approximately 8600 base pair AscI to AscI fragment of genomic HVT DNA. This region includes BamHI fragments 10 and 21, and approximately 1100 base pairs of fragment 6 and approximately 1300 base pairs of fragment 7. The XhoI site (Nucleotide #1339-1344; SEQ ID NO. 12) was used for the insertion and expression of foreign genes in HVT. (See FIG. 3B). The foreign DNA inserted into the XhoI site of HVT is as follows: The fragment is an approximately 3556 base pair SalI to HindIII restriction subfragment of the ILTV Asp718I genomic fragment #8 (10.6 kb).Plasmid 852-52.II4 was used in conjunction with other subgenomic clones according to the PROCEDURE FOR GENERATING RECOMBINANT HERPESVIRUS FROM OVERLAPPING SUBGENOMIC FRAGMENTS for the construction of recombinant HVT.

Detailed Description Text (216):
Plasmid 864-74.18 was constructed for the purpose of generating recombinant chimeric HVT/MDV vaccine expressing a foreign DNA sequence. The E. coli lacZ gene is expressed under the control of the PRV gX promoter. The HVT DNA is an AscI subclone

of cosmid 407-32.1C1 (see FIGS. 2 and 5). The cosmid was constructed by joining restriction fragments (Sambrooks, et al., 1989) from the following sources. The vector is an approximately 2000 base pair AscI fragment constructed from a 2000 base pair AatII to PvuII fragment of pNEB193 (New England Biolabs, Inc.) blunt ended with Klenow DNA polymerase and AscI linkers inserted. The HVT fragment is an approximately 8600 base pair AscI to AscI fragment of genomic HVT DNA. This region includes BamHI fragments 10 and 21, and approximately 1100 base pairs of fragment 6 and approximately 1300 base pairs of fragment 7. The XhoI site (Nucleotide #1339-1344; SEQ ID NO. 12) was used for the insertion and expression of foreign genes in HVT. (See FIG. 3B). The foreign DNA inserted into the XhoI site of HVT is as follows: Fragment 1 is an approximately 3556 base pair SalI to HindIII restriction subfragment of the ILTV Asp718I genomic fragment #8 (10.6 kb). Fragment. 2 is an approximately 413 base pair SalI to BamHI restriction sub-fragment of the PRV BamHI restriction fragment 10 (Lomniczi et al., 1984). Fragment 3 is an approximately 3010 base pair BamHI to PvuII restriction fragment of plasmid pJF751 (Ferrari et al., 1985). Fragment 4 is an approximately 754 base pair NdeI to SalI restriction sub-fragment of the PRV BamHI restriction fragment #7 (Lomniczi et al., 1984). Plasmid 864-74.18 was used in conjunction with S-HVY-145 according to the DNA TRANSFECTION FOR GENERATING RECOMBINANT VIRUS for the construction of recombinant chimeric HVT/MDV vaccine.

Detailed Description Text (241):
The MDV protective antigens within the unique short (gD, gE, and gI) elicit a protective immune response to MDV, while the virulence elements present in the unique long of MDV (55,56, 57) are replaced by the attenuating unique long sequences of HVT. The result is an attenuated virus vaccine which protects against Marek's disease. Multivalent protection against Marek's disease, infectious laryngotracheitis, infectious bursal disease, Newcastle's disease, or another poultry pathogen is achieved by inserting the ILTV gB,gD, and gI genes, the IBDV VP2 gene, the NDV HN and F genes, or an antigen gene from a poultry pathogen into an XhoI site converted to a PacI site or NotI site in the EcoR1 #9 (BamHI #10) fragment within the unique long region of HVT/MDV recombinant virus (FIGS. 2 and 5).

Detailed Description Text (249):
S-HVY-149 is a recombinant chimeric virus comprising a chimera of the Marek's disease virus short region and the herpesvirus of turkeys long region. S-HVY-149 is a recombinant chimeric viral vaccine that comprises foreign DNA from the infectious laryngotracheitis virus glycoprotein D (gD) and glycoprotein I (gI) genes inserted into an XhoI site in the EcoR1 #9 fragment within the unique long region of the chimeric virus. The ILT virus gD and gI genes are under the control of the ILT virus gD and gI promoters. The recombinant chimeric viral vaccine is useful against challenge with virulent Marek's disease virus and infectious laryngotracheitis virus.

Detailed Description Text (259):
S-HVY-152 is a recombinant chimeric virus comprising a chimera of the Marek's disease virus short region and the herpesvirus of turkeys long region. S-HVY-152 is a recombinant chimeric viral vaccine that comprises foreign DNA from E. coli lacZ gene and the infectious laryngotracheitis (ILT) virus glycoprotein D (gD) and glycoprotein I (gI) genes inserted into an XhoI site in the EcoR1 #9 fragment within the unique long region of the chimeric virus. The E. coli lacZ gene is under the control of the PRV gX promoter. The ILT virus gD and gI genes are under the control of the ILT virus gD and gI promoters, respectively.

CLAIMS:

11. The recombinant herpesvirus of turkeys--Marek's disease virus chimera of claim 7, wherein the antigenic polypeptide is infectious laryngotracheitis virus glycoprotein B (gB), infectious laryngotracheitis virus glycoprotein I (gI), or glycoprotein D (gD).